“一带一路”出版计划优秀出版物

Textbook for National Higher Education

全国高等学校教材

药理学实验教程

（英汉双语版）

Editors-in-Chief Hu Hao & Ban Tao

主编 胡浩 班涛

Pharmacology Experiment Course

(English-Chinese Bilingual Edition)

人民卫生出版社

PEOPLE'S MEDICAL PUBLISHING HOUSE

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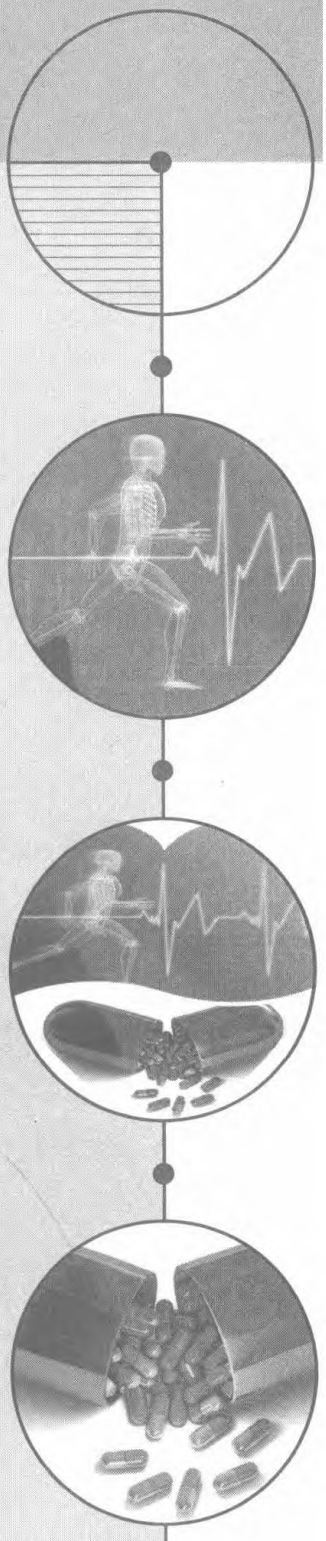

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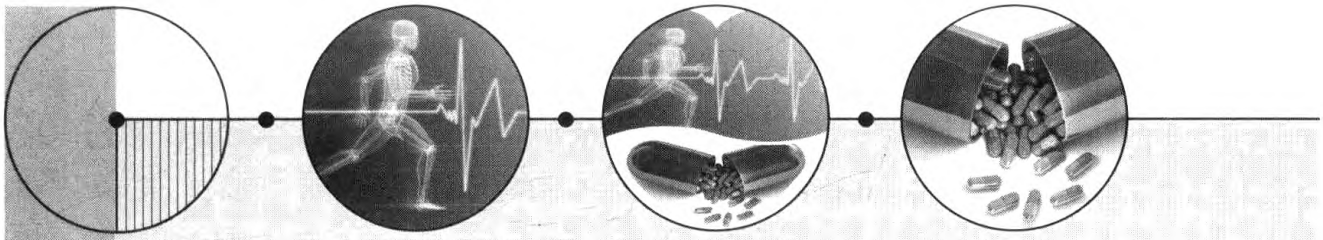


Preface

Pharmacology, a bridge course between clinical medicine and basic medicine, is a professional basic course required for medical students. Pharmacological experiment teaching, as an essential part of pharmacology course, is characterized by practicalness, intuitiveness, comprehensiveness and heuristic. It is also an important classroom activity for students to receive medical practice training and improve their practical ability.

Since 1990s, a large number of foreign students have received medical education in Chinese universities. Every year, thousands of foreign students pursue education in medicine and pharmacy in China. The vast majority of colleges and universities provide medical courses teaching for all foreign students in full English, including experimental teaching. However, due to lack of formal published materials, many colleges and universities have to use the lecture notes prepared by their own on pharmacology experiment, and the contents of lectures are relatively limited and outdated, which can no longer fully adapt to the rapid development of pharmacology and the needs of high quality teaching. Although the pharmacological experiment course of most medical colleges has been integrated into "functional experiment", there are still many colleges offering the experimental courses of pharmacology for the foreign students. The bilingual teaching advocated by the Ministry of education is an inevitable requirement to suit the development of the new era and the international integration, improving the quality of undergraduate teaching and enhancing the ability and quality of teachers and students at the same time. Therefore, it is of great significance to compile teaching materials for foreign students' education and bilingual teaching.

Pharmacology Experiment Course (English-Chinese Bilingual Edition) aims to provide students with a guidance material for learning and practicing basic knowledge, skills and methods of pharmacological experiments. This textbook adheres to the principles of

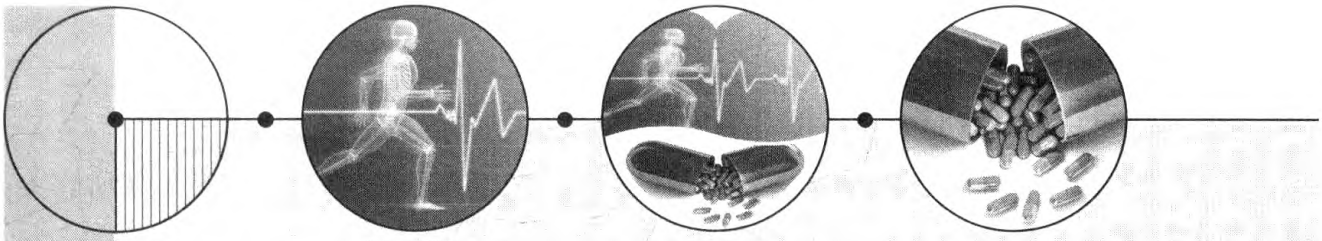
sticking to the basic theory, basic knowledge and basic skills, laying stress on ideology, science, advanced nature, heuristic and applicability, and aiming at specific targets, specific objects and specific restrictions. The teaching materials are written in English and Chinese. On the basis of introducing the experimental contents of each chapter, we add some basic knowledge of pharmacological experiments. We introduce the ethics and protection of laboratory animals, the methods for the capture and administration of animals, the use of common surgical instruments, and the writing requirements of laboratory reports. The latest educational ideas and educational concepts require students to change from passive acceptance to active knowledge acquisition. Carrying out innovative experimental teaching or exploring design can improve the comprehensive quality of students. A specific chapter is included to introduce experiment research training in this textbook. In order to further enhance the self-learning ability and innovative thinking ability on the basis of training operation ability of the students, we not only introduce the medical literature retrieval method, the basic principles and methods of experimental design, but also emphasize the key points of the experimental research plan implementation and the writing methods of the research papers.

This textbook is mainly used for pharmacology experiment teaching for foreign students of medical majors and domestic undergraduate pharmacology related teaching. It can also serve as a reference book for other academic users. This textbook is compiled by experts and teachers from a dozen medical colleges and universities who are engaged in pharmacology teaching, with rich teaching experience. In the process of publishing, the textbooks received strong support and help from the leaders and colleagues of the compiling units and People's Medical Publishing House, with regards to the highest respect and heartfelt thanks.

Although the autors have worked hard on the compilation of this textbook, due to limited experience and level, the omission in the teaching materials is unavoidable. Please enlighten us with your positive criticism and suggestions, so that we can have the opportunity to improve the compilation of this textbook in the future.

The Editorial Committee

May 2018



前　言

药理学是临床医学和基础医学之间衔接的桥梁课程，是医学各专业学生必修的专业基础课。药理学实验教学作为药理学课程的重要组成部分，具有实践性、直观性、综合性、启发性等特点，也是学生接受医学实践训练和提高实践能力的重要课堂。

自20世纪90年代开始，我国开始接收外国留学生来华进行医学教育，现每年已有几千名留学生在我国学习医药学。绝大多数学校的留学生授课采用全英文教学(包括实验课教学)，然而很多学校缺少正式出版教材，多沿用自己学校编写的实验课讲义，讲义内容相对局限、陈旧，已不能完全适应学科飞速发展和高质量教学需要。虽然目前我国绝大多数医学院校药理学实验课程已经整合为“机能实验学”课程，但在留学生教学中多数院校仍然开设“药理学实验课”。同时，教育部所倡导开展的双语教学也是适应新时代的发展，与国际接轨，提高本科教学质量，提高教师和学生能力与素质的必然要求。因此，编写适应留学生教学和双语教学的教材具有重要的意义。

《药理学实验教程(英汉双语版)》旨在为学生提供一部学习和实践药理学实验基本知识、技能与方法的指导教材。本教材在编写上遵循“三基、五性、三特定”原则：坚持以基础理论、基本知识、基本技能为重心，注重思想性、科学性、先进性、启发性和适用性，针对特定目标、特定对象、特定限制。教材以英文、中文双语表达为体例编写。内容上，在详尽介绍药理学各系统章节实验的基础上增加了药理学实验基本知识部分，包括实验动物伦理和动物保护、实验动物的捉拿给药方法、常用手术器械的使用以及实验报告的书写等。全新教育思想与教学理念强调学生学习要由被动接受变为主动获取知识，通过开展创新性实验教学或探索设计性实验提高学生的综合素质与能力，因此我们在教材中还增加了医学实验研究训练内容，不仅介绍了医学文献检索方法、实验设计的基本原则及常用方法，而且还强调了实验研究计划实施的注意要点以及研究论文的撰写方法等，以期在加强学生动手操作能力的基础上，进一步提升学生自主学习能力和创新思维能力。

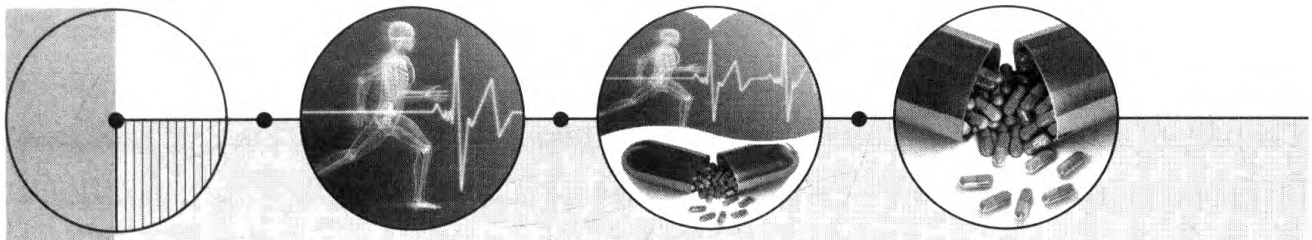
本教材主要面向医药院校各专业留学生药理学实验教学以及国内本科生药理学相关教学使用，也可作为其他人员的参考用书。教材由全国十余所高等医药院校长期从事药理学

教学一线具有丰富教学经验的专家、教师共同编写完成，凝聚了全体编写人员的智慧和心血。教材在出版过程中，得到了各参编单位和人民卫生出版社领导、同仁的大力支持和帮助，在此致以崇高的敬意和衷心的感谢。

尽管全体编写人员尽心努力，但是由于经验和水平有限，深感教材疏漏之处在所难免，敬请广大师生和读者赐教指正，积极建言献策，以便今后不断完善和提高。

《药理学实验教程》编委会

2018 年 5 月



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Section 1 Ethics and protection of experimental animals

The use of animals in biomedical research is a privilege granted by society, and the rules and regulations that govern this usage are in place to ensure the welfare of the laboratory animal subjects. To find a balance between achieving both scientific and animal welfare objectives, this is accomplished by incorporating principles for more ethical use of animals in research, teaching and testing.

1. Ethics principles

It is ultimately the responsibility of each investigator to comply with regulations for the welfare and safety of the animals involved in any research project. This includes better housing and improvements to procedures which minimize pain and suffering and/or improve animal welfare, the use of well-defined endpoints, the proper use of pharmacological interventions and the use of other pain-alleviating methods. Furthermore, the investigators are required to take responsibility for the following principles: (1) Research should be based on animal health, the advancement of knowledge, or for the good of society. (2) Appropriate species, quality and number of animals should be used. (3) Pain and distress should be minimized. (4) Appropriate sedation, analgesics and anesthetics should be used. (5) Defined end points should be established. (6) Appropriate animal husbandry directed by qualified personal should be provided. (7) Experiments on live animals should be conducted by or under the supervision of experienced personal.

2. 3Rs principles

Animal experiment design should follow the 3R principles: replacement, reduction and refinement. Replacement: the use of animals with alternative techniques, or avoid the use of animal altogether. Reduction: the number of animals used to a minimum, to obtain information from fewer animals or more information from the same number of animals. Refinement: the way experiments are carried out, to make sure animals suffer as little as possible.

3. Animal welfare principles

To ensure the survival of experimental animals (including transportation) with the basic rights: (1) no hunger and thirst; (2) living comfort; (3) no pain and illness; (4) living without fear

and sadness; (5) expressing innate behavior. These five basic principles are the five criteria for protecting animal welfare.

(Li Dongling)

Section 2 General knowledge of animal experiments

1. Common laboratory animals

1.1 Toad

Toads are amphibious animals and characterized by dry, leathery skin, short legs, and parotoid glands. As adults, toads potentially can live a long time. Toad is used extensively for experimental purposes for several decades, especially as subjects for dissection in teaching institutions. The sciatic nerve, gastrocnemius muscle and heart are separated in the physiological and pharmacological experiments (Figure 1-1).

Figure 1-1 Toad

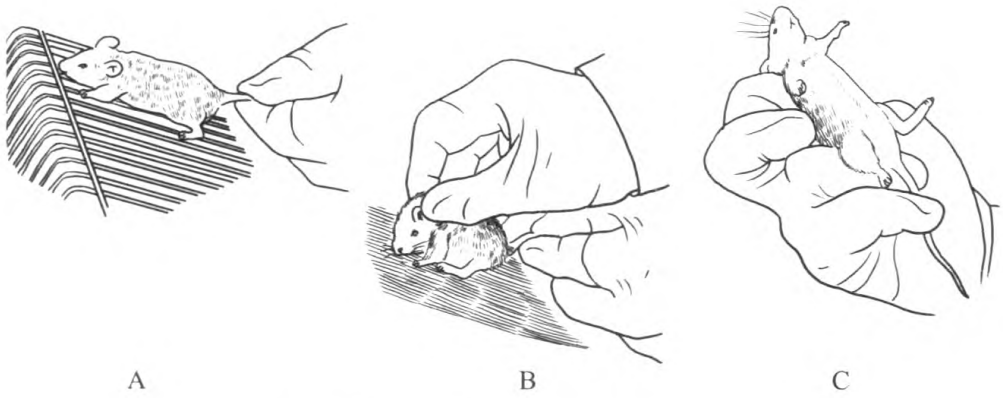
Pithing (decerebration followed by spinalisation) is one usual procedure of euthanasia. The pithing rod is stainless steel or any non-ferrous metal and a diameter of the pithing rod is less than 2 mm. Toad is held firmly and inserted into the middle spot between the first vertebra and the occipital region of the cranium by the pithing rod. Then, move the probe into the cranial vault and destroy the brain. Finally, turn the probe around into the vertebral canal and sever the spinal cord. If the above procedure is successful, the sensory perception (corneal reflex and pinch the leg) of toad will disappear and the toad legs become completely limp (paralysis of skeletal muscle).

1.2 Mouse

Mice are very active. An adult mouse is 6-8 weeks old with body weight at 18-20 g (Figure 1-2). The life span is 1.5-3 years. It is reported that 70% of experimental animals used in pharmacological researches are mice.

Figure 1-2 Mouse

Remove the mouse from the cage by gently grasping the tail with left hand and place the mouse on a wire-bar cage lid to permit grasping. Approach the back of the neck from the rear with right hand. Firmly grasp the skin behind the ears with thumb and index finger. With remaining fingers gently grasp the loose skin along the mouse's spine. Transfer the tail from the preferred hand to beneath the little finger of the hand holding the scruff of the neck (Figure 1-3).



A B C

Figure 1-3 Handling the mouse

1.3 Rat

Sprague-Dawley rats are originated from the Sprague Dawley farm in 1925, and they are derived from Wistar rats. They are typical rodents, with continuously growing incisors. Rats should be fed a commercial pelleted rat or rodent diet and water *ad libitum*. An adult rat is 10 weeks old and weigh 220-300 g. The life span is 2.5-3.5 years.

Rats can be removed from their cages by briefly picking them up at the base of the tail. Grasp the skin behind the ears with thumb and index finger. With remaining fingers gently grasp the loose skin along the rat's spine (Figure 1-4).

A B

Figure 1-4 Rat and handling

1.4 Rabbit

The New Zealand white rabbit is commonly used in research, and the body weight is about 2-3 kg. The life span is 5-6 years. Grasp the back fur with the right hand, and gently lift the animal. Then hold the buttocks with the left hand, so that the weight of the rabbit falls mainly in the palm of the left hand, and then fixed according to the experimental requirements (Figure 1-5).

2. Administration routes of animals

2.1 Oral administration (or intragastric injection, i.g.)

Oral gavage is used when some drugs must be administered orally or directly into the stomach. The specially designed gavage rounded-tip needle is used. This needle is first measured

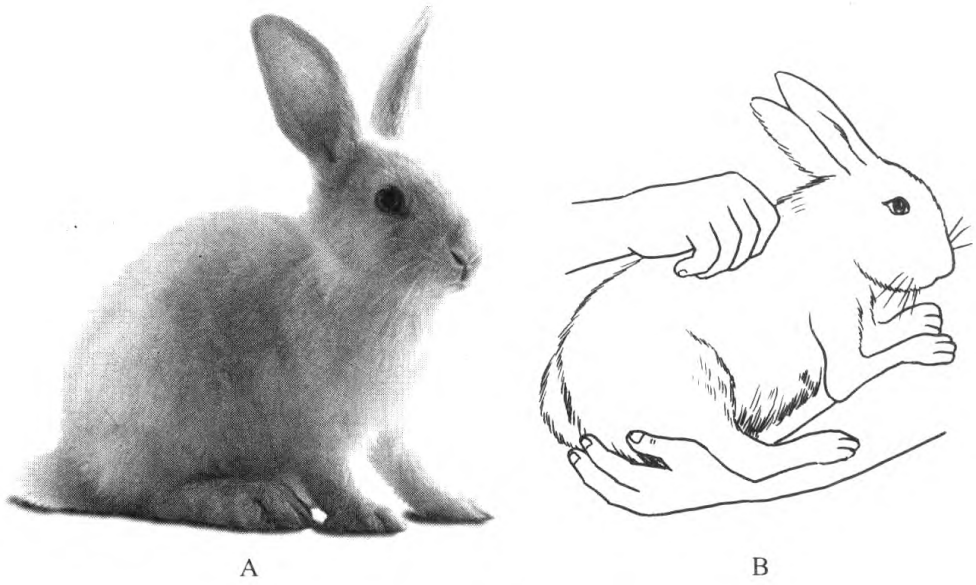


Figure 1-5 Rabbit and handling

alongside the animal's body to determine the approximate distance "needle" will need to be inserted to reach the animal's stomach.

2.1.1 Mouse

The needle tip is placed in the mouth via the diastema (space between the incisors and molars) and slid toward the throat. Utilizing the animal's own swallowing reflex the needle is passively advanced down the esophagus until it is fully inserted to the level of the stomach. The contents of the syringe are then administered slowly. The recommend volume delivered by oral gavage usually is 0.1-0.2 ml/10 g body weight (Figure 1-6).

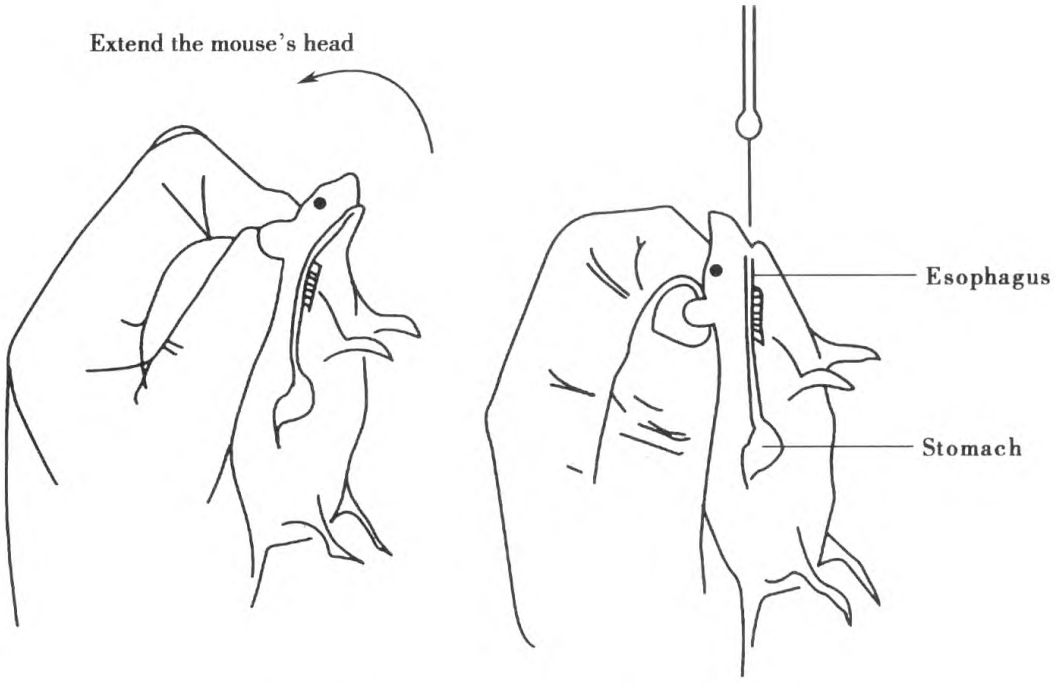


Figure 1-6 Intragastric administration in mouse

2.1.2 Rat

The left hand wears the protective gloves to hold the rat. The right hand puts the syringe gavage needle into the mouth from its mouth angle, and then the needle is gently entered into the esophagus along the back wall of the pharynx. When the insertion is smooth, without resistance, to insert the needle deeper into stomach and inject the liquid. The insertion of the trachea should be avoided. The volume of oral gavage usually is 1-2 ml/100 g body weight.

2.1.3 Rabbit

In general, the mouth opener and pediatric catheter are used to gavage the rabbits. The mouth opener is a $2\times2\times10$ cm^3 piece of wood or bamboo slice, which is spindle shaped and is vertically opened with a circular hole of 6-8 mm diameter. The forefeet and roots of the ears of the rabbit should be hold tightly and put upward, the hip of the rabbit can be stuck between thighs of handler. The mouth opener is placed between the upper and lower palate teeth of the animals. The two ends of mouth opener are fixed by the rope or by the hand. The catheter is inserted into the esophagus through the small round hole of the opener and slowly into the esophagus into the stomach along the posterior wall of the pharynx. After the injection, a small amount of water is used to rinse the residual fluid in the tube, and then the catheter is pulled out.

2.2 Intravenous administration (i.v.)

2.2.1 Mouse and rat

The mouse or rat is either placed in the restrainer and the tail is immersed in warm water (40-45 ℃) or swabbed with 75% alcohol on a gauze sponge in order to dilate the vessels. Insert the needle parallel to the tail vein penetrating 2-4 mm while keeping the bevel of the needle face upwards. The solution is then injected slowly and no resistance should be felt. If the needle is certainly not in the vein but in the surrounding tissue, it must be moved out and a new try must be made. When the intravenous administration is finished, the injection site must be pressed firmly with a swab. The recommended volume usually is 0.1-0.2 ml/10 g body weight (Figure 1-7).

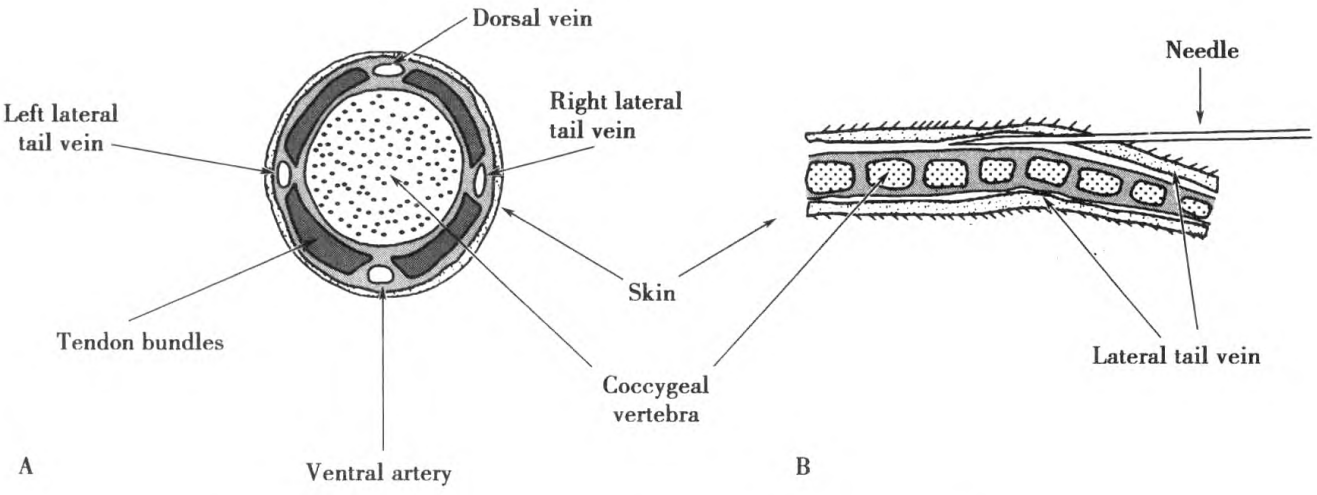


Figure 1-7 Intravenous administration via the tail vein in mince

2.2.2 Rabbit

Injections are administered to rabbits in the auricular vein, since it is large enough, linear course and readily accessible. The needle is inserted into the vein in the direction of the ear root. If blood flows in the syringe, the needle was put in the vein. When the intravenous administration is finished, the injection site must be pressed firmly with a swab (Figure 1-8).

Figure 1-8 Intravenous administration via the auricular vein of in rabbits

2.3 Intraperitoneal injection (i.p.)

The mouse, rat or rabbit is restrained and held in a supine position with its posterior end slightly elevated or the head can be tilted lower than the body. The needle is pierced in the direction of 45 degree angle with the abdomen. When the needle penetrate into the abdominal cavity, there is a sense of loss, and the syringe was pumped back. If there is no abnormal fluid when back pumping, it can be administered. Mice, rats and rabbits are the similar practice.

2.4 Subcutaneous injection (s.c.)

Subcutaneous injection is relatively easy. The mice and rabbits are usually on the back, and the rats are in the left lower abdomen. The skin of the injection site is pulled up, and the needle is pierced into the skin to inject the medicine. When the needle is pulled out, the needle position is pinched by fingers to prevent the leakage of the liquid.

3. Collection methods of animals body fluid

3.1 Blood collection

3.1.1 Saphenous vein blood collection

This technique has been usually used in mice and rats, and small blood volume (0.2-0.3 ml in mice; up to 3 ml in rats) may be taken. The animal is placed in a suitable restrainer, extended the hind leg, the back of the hind leg is shave until saphenous vein is visible and the area wiped with alcohol. The saphenous vein is on the lateral aspect of the tarsal joint. The vein is raised by gentle pressure above the knee and the vessel is punctured using the syringe with the smallest needle that enables sufficiently rapid blood that enables sufficiently rapid blood withdrawal without haemolysis. After blood has been collected, the punctured site is pressured over until stopped further bleeding. It is not necessary to anesthetize and so is particularly suitable for repeated blood sampling as in scientific research.

3.1.2 Lateral tail vein blood collection

It is similar to saphenous vein blood sampling method, but the amount of blood collection is less than that of saphenous vein (0.1-0.15 ml in mice; up to 2 ml in rats). Anesthesia is not necessary. To fix the animal with the mouse box and expose the tail of the mouse. The tail end is

immersed into the warm water of 45-50℃ for several minutes or is wiped repeatedly with 75% alcohol. After the tail vein is congested obviously, it is needled and the blood sample is collected by a capillary tube or dropping into a container. This route is particularly suited for repeated blood sampling. It is necessary for vasodilatation by warming that will be to promote bleeding.

3.1.3 Auricular vein/middle auricular artery blood collection

Blood sampling from the auricular vein or middle auricular artery is commonly used in rabbits. The fur is shaved in the area of auricular vein and then to puncture the vein and collect the blood into a tube. For the removal of larger amounts of blood (5-10 ml), the middle auricular artery in rabbits can be used, but afterwards it must be compressed for at least 2 min to prevent continuing bleeding and haematoma. The animal should be checked for persistent bleeding 5 and 10 min later. Repeated samples can be taken from this artery using an indwelling cannula. In addition, if the rabbit is anesthetized and intubated via jugular vein/common carotid artery, it is easy to take the blood sample from the cannula.

3.1.4 Orbital venous plexus blood collection

Orbital venous plexus blood collection is a common blood sampling method in mice and rats for long time. But because of its large side effects and the 3R principles of animals, it has now been replaced by saphenous vein blood sampling and less used. It should be used under general anaesthesia and not be repeated on the same eye for at least two weeks. The animal is restrained, the neck gently scruffed and the eye made to bulge. Insert a capillary pipet into the inner canthus, directing the tip at a 45° angle toward the middle of the eye socket. Gently rotate the pipet until the vein is broken and blood enter the pipet. Bleeding usually stops immediately when the pipet is removed. It may be necessary to apply gentle pressure on the eyeball to close the eye for a moment. The volume of blood sampling usually is 0.2-0.3 ml in mice, and 0.5~1.0 ml in rats.

3.1.5 Abdominal aorta blood collection

Abdominal aorta is appropriate for mice and rats blood collection. Abdominal aorta blood collection is a suitable technique to obtain a single, large, good-quality blood sample under terminal anesthesia. A sample size of 0.6-1.2 ml (mouse) or 10-15 ml (rat) can be collected from abdominal aorta. Blood is collected from the abdominal aorta via a laparotomy. Gentle push aside bowel and pressure the artery to dilate the vessel. Blood should be withdrawn slowly with syringe. Deep surgical anesthesia is necessary.

3.1.6 Notes and tips for blood collection

The excessive blood collection or too frequent blood sampling can affect animal health, leading to anemia and even death. The maximum safe blood sampling volume is shown in Table 1-1. For serum, whole blood is allowed to clot naturally and the supernatant is retained, with no anticoagulants added. However, for plasma, which is the non-clotted fraction of blood, these processes are dampened by the addition of so-called anticoagulants which are added straight away. Sodium citrate, EDTA and heparin are commonly chosen examples. The sample should be mixed with anticoagulant rapidly to prevent clotting in the tube. (1) 10% EDTA·Na_2: 0.1 ml EDTA·Na_2 (disodium ethylenediaminetetraacetic acid) prevents 5-10 ml blood clotting. (2) 1%